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Health-Related Quality of Life in Japanese Patients Treated with Intensity Modulated Radiotherapy (IMRT) for Localized Prostate Cancer: Three-Year Longitudinal and Cross-Sectional Evaluations

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ABSTRACT

Objective: To evaluate the health-related quality of life (HRQOL) in patients with localized prostate cancer undergoing treatment with IMRT with or without androgen deprivation therapy (ADT).

Method: Changes in physical (PCS) and mental (MCS) summary scores were evaluated at eight time points up to three years after IMRT using SF-8 questionnaires, employing longitudinal and cross-sectional analyses. The effect of the combination of ADT and patient age on the PCS and MCS was also evaluated.

Results: A significant increase in MCS was observed longitudinally after IMRT in all patients, with no change in PCS. Significant increases in MCS were observed in patients receiving IMRT alone and in those receiving IMRT in combination with ADT. However, no change in PCS was observed, regardless of whether ADT was administered. A significant increase in MCS was observed regardless of whether ADT was administered in combination, but no change in PCS. PCS were higher in younger patients than in older patients, regardless of the ADT combination used. However, the difference was more pronounced in patients treated with IMRT alone. Patients treated with IMRT alone had a lower baseline MCS than those receiving combined ADT. Nevertheless, the MCS increased significantly at 6 months after IMRT, eliminating the difference between the two groups.

Conclusions: While IMRT reduces adverse events and minimizes the deterioration in HRQoL in patients with localized prostate cancer, changes in PCS and MCS are influenced by ADT and patient age.

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Introduction

The increase use of PSA testing has led to rise in the number of localized prostate cancer patients worldwide. In Japan, the annual incidence of prostate cancer in 2021 is approximately 96,000 cases, making it the leading cancer among Japanese men.

There are several treatment options for localized prostate cancer, including radical prostatectomy, external beam radiotherapy, brachytherapy, androgen deprivation therapy (ADT), and active surveillance. When choosing treatment modalities, consider the outcomes as well as the patient's health-related quality of life (HRQOL). However, it is difficult to measure the burden and change in HRQOL experienced by patients due to adverse events caused by various treatment modalities through the objective assessment of these events by medical professionals. Therefore, many various methods of self-assessment for these events have been developed using questionnaires.

The UCLA Prostate Cancer Index (PCI) is a disease-specific quality-of-life scale for patients with localized prostate cancer that is widely used internationally [1]. Kakei et al. validated and adapted the scale for use in Japan, where it is now widely used to evaluate prostate cancer treatment modalities [2].

The comprehensive Health-Related Quality of Life Questionnaire: SF-36 is a HRQOL questionnaire that was developed in the United States in the 1980s as part of the Medical Outcomes Study (MOS) [3]. The MOS was a large-scale outcomes research project targeting patients with major chronic diseases. SF-36 has gained attention as a method of measuring patient' s national standard objective health. It is a scale that include psychosocial aspects. It has been translated into more than 170 languages and widely used internationally. A Japanese version was developed by Fukuhara et al. to show national standard values for Japanese people [4]. Many papers that have evaluated general HRQOL in patients with prostate cancer assessed using S-36 have been already published [5-9].

A further reduced version of the SF-36, the Medical Outcomes Study 8-item Short Form Health Survey (SF-8), has been developed. The SF-8 consists of eight subscales (constructs) of the SF-36, each with a corresponding question. The small number of questions reduces the burden on patients and allows them to evaluate HRQOL. The SF-8 Japanese version is now available

and linked to the Japanese version of the Expanded Prostate Cancer Index Composite (EPIC) [1,2,10-13].

The SF-8 contains psychometrically based physical and mental health summary measures, scoring eight domains, and two component summaries, which are calculated by weighing each SF-8 item using a norm-based scoring method given in the instrument guidelines [14]. Higher domain scores, summary score for physical health (PCS), and that for mental health (MCS), indicate better health status.

Many reports about HRQOL in patients with localized prostate cancer treated with various treatment modalities including external radiation therapy have been published [5-6,13,15-17]. However, in recent years, the rapid advancement of radiation therapy technology has led to the widespread adoption of intensity-modulated radiation therapy (IMRT) in Japan. This has resulted in a significant increase in the number of patients with localized prostate cancer who opt for radiation therapy. IMRT reduces adverse events such as rectal, bladder, and urethral complications. Nevertheless, the impact of IMRT on the HRQOL of patients with localized prostate cancer has not yet been adequately evaluated. Additionally, since some patients undergo androgen deprivation therapy (ADT) alongside radiation therapy, the effects of ADT on the HRQOL of patients who have undergone IMRT have not yet been sufficiently evaluated.

Therefore, we analyzed the longitudinal and cross-sectional impact of IMRT with or without ADT on the HRQOL of Japanese patients with localized prostate cancer by using the SF-8, a patient-reported outcome measure. We also analyzed the impact of patient age on HRQOL, with the understanding that this is an important factor in understanding the needs of our patients.

Material and Methods

Patients and Tumors Characteristics

A total of 267 consecutive patients with localized prostate cancer who were treated with IMRT with or without ADT at a single institute were enrolled in the study. These patients were referred to our department for IMRT between July 2016 and August 2021and followed up at least for three years after IMRT. This study was approved by the Institutional Ethics Review Board (Study number: 14-003, BOE-38-001_202506-01). All study participants provided written informed consent, and the study protocol was conducted in accordance with the World Medical Association's Code of Ethics (Declaration of Helsinki).

The average age ± standard deviation (SD) was 71.5 ± 5.9 years old (range 53-82 years old). Table 1 shows the characteristics of the tumors. For T factor, 2 patients had T1b, 120 had T1c, 71 had T2a, 7 had T2b, 23 had T2c, 30 had T3a and 14 had T3b disease. Out of 267 patients, 193 (72.3%) had stage I disease.

Table 1: Tumor Characteristics of Patients with Localized Prostate Cancer

Tumor Characteristics	No. of Patients (%)
T Factor	
T1b	2 (0.8)
T1c	120 (44.9)
T2a	71 (26.6)
T2b	7 (2.6)
T2c	23 (8.6)
T3a	30 (11.2)
T3b	14 (5.3)
Stage	
I	193 (72.3)
II	30 (11.2)
III	44 (16.5)
Gleason Score :	
3+3	92 (34.5)
3+4	41 (15.3)
3+5	4 (1.5)
4+3	56 (21.0)
4+4	41 (15.3)
4+5	28 (10.5)
5+4	5 (1.9)
Serum PSA Valure :	
PSA < 5	20 (7.5)
5 ≦ PSA < 10	127 (47.5)
10 ≦ PSA < 20	72 (27.0)
20 ≦ PSA	48 (18.0)
D'Amico clinical risk classification	
Low Risk	64 (24.0)
Intermediate Risk	93 (34.8)
High Risk	110 (41.2)
Pathology	
Adenocarcinoma	266 (99.6)
Neuroendocrine cancer	1 (0.4)

The most common Gleason score (GS) was 3+3, which was observed in 92 patients. Next was 4+3, observed in 56 patients, followed by 3+4 and 4+4, each observed in 41 patients. Twenty patients had serum PSA levels of 5 ng/mL or less, 127 patients had levels between 5 and 10 ng/mL, 72 patients had levels between 10 and 20 ng/mL, and 48 patients had levels of 20 ng/mL or more. Using the D'Amico clinical risk classification, 64 patients were classified as low risk, 93 as intermediate risk, and 110 as high risk.

All patients were pathologically classified as adenocarcinomas, except for one patient of neuroendocrine cancer.

HRQOL Assessment

The summary score in SF-8 is obtained by the weighted scores for each item and adding a constant. The calculation formula is designed so that the average summary score of Japanese people is 50. Therefore, SF-8 scores above and below 50 are above and below average, respectively, in the general Japanese population. Higher domain scores, PCS and MCS, indicate better health status [10-13].

We evaluated changes and recovery patterns for patients subject to analysis over time of average PCS and average MCS at the start of IMRT (baseline) and 4 weeks, as well as 1, 3 and 6 months, and, 1, 2, and 3 years after IMRT, using the SF-8 questionnaire. We also analyzed the effects of ADT and/or patient age on PCS and MCS by using both longitudinal and cross-sectional approaches. The effects of ADT on PCS and MCS were compared between a short-term combination group (less than one year) and a long-term combination group (more than one year). Those of age on PCS and MCS were dividing the patients into two groups: 102 patients aged 70 years or younger (younger patients) (Mean age ± SD: 65.40 ± 4.37) and 165 patients aged 71 years or older (older patients) (Mean age ± SD: 75.30 ± 2.69).

Treatment

Androgen Deprivation Therapy (ADT)

Table 2 demonstrated treatment characteristics of patients. ADT was administered according to the risk classification as follows: no ADT to patients in the low-risk group, 4 - 6 months neoadjuvant ADT to those in the intermediate-risk group, and 4 - 6 months neoadjuvant ADT and 24 - 36 months adjuvant ADT to those in the high-risk group. In the first half the study, however, patients in the intermediate-risk group with a GS of 3+4 were treated with IMRT alone without ADT. ADT mainly comprised administration of a luteinizing hormone-releasing hormone agonist plus a nonsteroidal or steroidal antiandrogen. A total of 187 patients (70.0%) received ADT in combination with IMRT. One hundred and four of these patients (55.6%) received ADT for more than one year (long-term ADT group) and 83 patients (44.4%) received ADT for less than one year (short-term ADT group).

Table 2: Treatment Characteristics of Patients with Localized Prostate Cancer

Treatment	No. of Patients (%)
Androgen Deprivation Therapy (ADT)	
No	80 (30.0)
Yes	187 (70.0)
Less than one year	83 (44.4)
More than one year	104 (55.6)
Intensity Modulated Radiation Therapy (IMRT)	
6 Gy/3 Fr.	1 (0.4)
16 Gy/8 Fr.	1 (0.4)
69 Gy/23 Fr.	1 (0.4)
70Gy/35 Fr.	1 (0.4)
74 Gy/37 Fr.	257 (96.3)
78 Gy/39 Fr.	6 (2.2)
Loss of Follow-up	5 (1.9)
Discontinued Radiotherapy	2 (0.7)

Intensity Modulated Radiotherapy (IMRT)

As shown in Table 2, the total radiation dose was 74 Gy in 37 fractions. IMRT was performed daily. For one patient who had neuroendocrine cancer that was radioresistant, 69 Gy was administered every other day in 23 fractions. The dose was increased to 78 Gy for six patients in the highest-risk group in latest period of this study. IMRT was completed as scheduled, except for two patients: one in which another cancer was detected, and one in which the patient refused treatment. The planning target volumes and OARs were delineated by two radiation oncologists on the CT slices by using CT images superimposed with T2-MR images and the contouring tool of Pinnacle 3 treatment planning system v9.10 (Philips Healthcare, Fitchburg, WI).

Various volumes of interest were defined: GTV (prostate), CTV (prostate and proximal seminal vesicle), and PTV (CTV+8 mm margin except for 5 mm posterior) were outlined as well as organs at risk (OARs), including rectum; bladder, penile bulb and the left and right head of femur were outlined. The bladder and rectum were defined by contouring the whole organ, including the contents. After simulation and contouring, the target volumes were planned on Pinanacle3 using the Convolution Superposition Algorithm. All plans were done using 10 MV photons. The dose was delivered using volumetric modulated arc therapy (VMAT), a type of IMRT.

Throughout the IMRT period, laxatives were administered to eliminate gas and feces in the rectum and keep the prostate in a constant position. This was confirmed using cone beam CT at the beginning of each irradiation session. Additionally, ultrasound was used to confirm the presence of 150-200 ml of urine in the bladder to maintain a constant size before irradiation began each time.

Treatment Outcomes

As shown Table 3, PSA failure was the most common cause of recurrence (16 patients), followed by bone metastasis (4 patients) during the three-year observation period.

Table 3: Recurrence Pattern of the Tumor

Recurrence Pattern	No. of Patients (%)
PSA failure	16 (6.0)
Lymph node metastases	1 (0.4)
Bone metastases	4 (1.5)
Lung metastases	1 (0.4)

According to RTOG/EORTC criteria, there were no grade 2 or higher acute genitourinary or gastrointestinal toxicities. Late toxicities are shown in Table 4. Only one patient developed grade 3 genitourinary toxicity.

Table 4: Late Toxicity According to RTOG/EORTC Criteria

Late Toxicity	No. of Patients (%)
Genitourinary	
Grade 1	16 (6.0)
2	2 (0.8)
3	1 (0.4)
Gastro-interstinal Tract	
Grade 1	14 (5.2)
2	2 (0.8)

Statistical Analysis

We performed unpaired two-tailed t-tests to analyze the average values of the PCS and MCS between two groups at each observation time point. Statistical significance was set at $p < 0.05$ for all statistical analyses. All analyses were performed using Microsoft Excel for Windows, version 16.26 (Microsoft Corporation, Redmond, WA, USA).

Results

Longitudinal Changes of PCS and MCS in all Patients

Figure 1 demonstrates the longitudinal evaluation of PCS and MCS in all patients.

There were no significant longitudinal changes in PCS compared to the baseline score at the seven evaluation points, although the baseline PCS was slightly lower at 48.78 ± 6.84 compared to the mean score for Japanese men.

The baseline MCS was the same as the average score of Japanese men (50.04 ± 6.18). However, the MCS increased significantly at 3 months (51.18 ± 5.40, p = 0.026) and 6 months (51.58 ± 5.04, p = 0.0021) after IMRT.

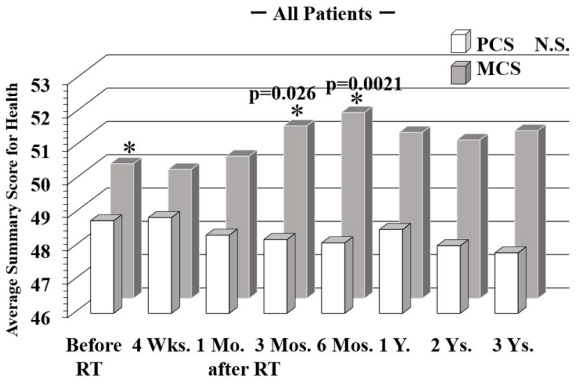


Figure 1: Longitudinal Evaluations of Average Summary Scores for Physical Health (PCS) and Mental Health (MCS) in All Patients (A comparison of the baseline score at the start of Intensity Modulated Radiotherapy (IMRT) and the scores at each evaluation point)

N.S: No statistically significant changes longitudinally compared with baseline

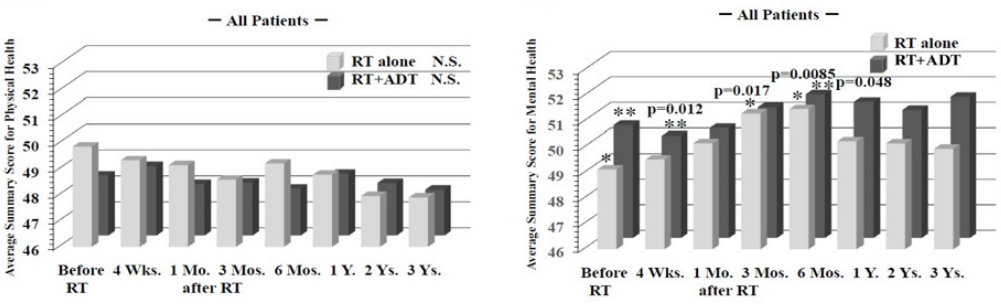
Effect of ADT on Longitudinal and Cross-Sectional Changes of PCS and MCS

Difference in PCS and MCS between Patients Treated with IMRT alone and Patients Treated with IMRT Combined with ADT

As shown in Figure 2A, PCS showed no significant difference up to three years in patients treated with IMRT alone, but gradually declined from baseline. No longitudinal change was observed in patients treated with IMRT combined with ADT. When comparing PCS of patients treated with IMRT alone and patients treated with IMRT combined with ADT, the IMRT alone group had higher scores at all measurement points, including the baseline measurement. Cross-sectionally, however, there was no significant difference between the two groups.

In patients treated with IMRT alone, MCS increased significantly at 3 months (49.14 ± 6.36 vs. 51.31 ± 5.46, p = 0.017) and 6 months (49.14 ± 6.36 vs. 51.48 ± 4.47, p = 0.0085) after IMRT, compared with the baseline score (Figure 2B). The MCS of patients who received RT combined with ADT decreased significantly once at 4 weeks (50.43 ± 6.08 vs. 50.02 ± 5.92, p = 0.012), then increased significantly 6 months after IMRT (50.43 ± 6.08 vs. 51.63 ± 5.29, p = 0.048).

The cross-sectional analysis revealed that MCS scores were higher in patients treated with IMRT combined with ADT at all assessment points. However, no significant difference was observed compared to patients treated with IMRT alone.

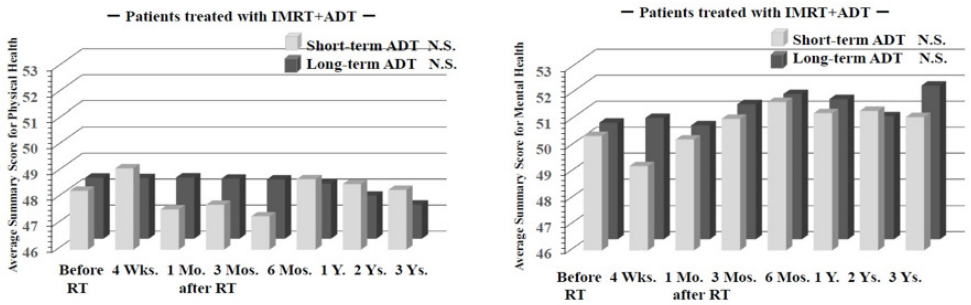


2A: Average Summary Scores for Physical Health (PCS) 2B: Average Summary Scores for Mental Health (MCS)

Figure 2: Longitudinal and Cross-Sectional Evaluations of Average Summary Scores for Health in Patients treated with Intensity Modulated Radiotherapy (IMRT) alone and IMRT combined with Androgen Deprivation Therapy (ADT)
N.S: No statistically significant changes longitudinally compared with baseline

Administration Period of ADT
Regardless of the duration of ADT, PCS levels remained stable over 3 years compared to the baseline score. However, a slight decrease in PCS was observed from 1 to 6 months after IMRT in patients receiving short-term ADT. (Figure 3A)

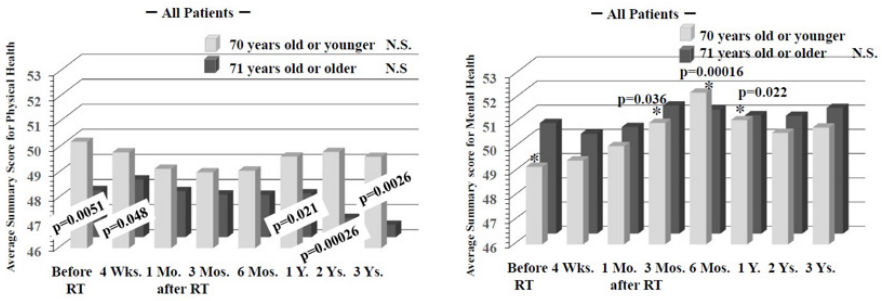
There were no statistically significant longitudinal changes in MCS for patients receiving short-term or long-term ADT at any evaluation point, including baseline score. (Figure 3B) However, MCS decreased slightly in patients treated with short-term ADT 4 weeks after the start of IMRT.



3A: Average Summary Scores for Physical Health (PCS) 3B: Average Summary Scores for Mental Health (MCS)

Figure 3: Longitudinal and Cross-Sectional Evaluations of Average Summary Scores for Health according to Administration Period of Androgen Deprivation Therapy (ADT) in Patients treated with Intensity Modulated Radiotherapy (IMRT) combined with Androgen Deprivation Therapy (ADT)
N.S: No statistically significant changes longitudinally compared with baseline

Effect of Patients Age on Longitudinal and Cross-Sectional Changes of PCS and MCS
All Patients
Figure 4 A shows longitudinal changes in PCS by age as well as cross-sectional changes across ages. In younger patients, the PCS decreased slightly over 6 months (49.01 ± 6.16), but then recovered to nearly baseline score (49.64 ± 6.64). Over the 3-years study period, the PCS scores of older patients gradually worsened without reaching statistical significance, and no recovery to baseline score was observed.



4A: Average Summary Scores for Physical Health (PCS) 4B: Average Summary Scores for Mental Health (MCS)

Figure 4: Longitudinal and Cross-Sectional Evaluations of Average Summary Scores for Health according to Age in All Patients
N.S: No statistically significant changes longitudinally compared with baseline

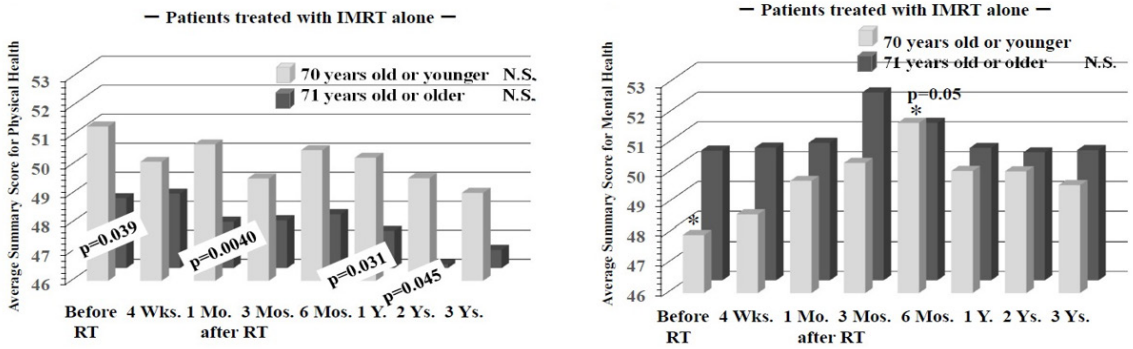
A cross-sectional comparison of PCS between younger and older patients revealed that younger patients had significantly higher PCS than older patients at the following time points: baseline score ($p = 0.051$), 4 weeks ($p = 0.048$), 1 year ($p = 0.021$), 2 years ($p = 0.00026$), and 3 years ($p = 0.026$).

Figure 4B shows longitudinal changes in MCS by age as well as cross-sectional changes across ages. In older patients, there was no change in MCS over 3 years compared to baseline. However, the MCS increased significantly at 3 months 51.01 ± 5.41, $p = 0.036$), 6 months (52.26 ± 4.41, $p = 0.00016$), and 1 year (51.13 ± 5.02, $p = 0.022$) compared with the baseline score (49.20 ± 6.63) for younger patients.

The baseline MCS of younger patients was only slightly lower than that of older patients (49.20 ± 6.63 vs. 50.57 ± 5.85, $p = 0.088$). There were no differences in MCS between younger and older patients, except for a slightly lower score for younger patients at baseline (49.20 ± 6.63 vs. 50.57 ± 5.85, $p = 0.088$), and a slightly higher score at 6 months after IMRT (52.26 ± 4.41 vs. 51.13 ± 5.39, $p = 0.074$), which showed significant trend.

Patients Treated with IMRT Alone

Longitudinal and cross-sectional changes in PCS by age in patient with IMRT alone is shown in Figure 5A. PCS scores remained consistently high in the younger patients from baseline to 3 years after IMRT. However, no statistically significant longitudinal changes were observed in either the younger or elderly patients.



5A: Average Summary Scores for Physical Health (PCS) 5B: Average Summary Scores for Mental Health (MCS)

Figure 5: Longitudinal and Cross-Sectional Evaluations of Average Summary Scores for Health according to Age in Patients treated with Intensity Modulated Radotherapy (IMRT) alone
N.S: No statistically significant changes longitudinally compared with baseline

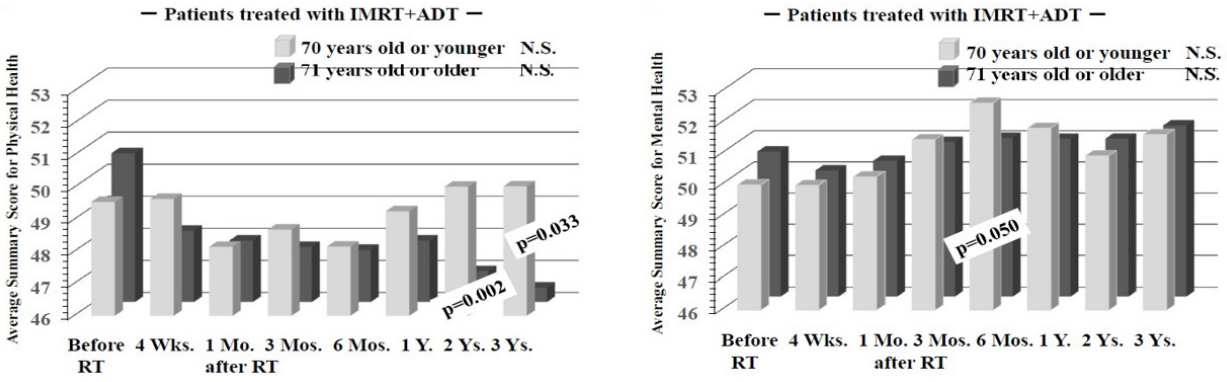
The cross-sectional analysis revealed that PCS scores for younger patients were significantly higher than those for older patients at baseline (51.32 ± 5.46 vs. 48.41 ± 6.84, $p = 0.039$) and at 1 month (50.70 ± 4.00 vs. 47.60 ± 5.15, $p = 0.0040$), 1 year (50.24 ± 5.33 vs. 47.29 ± 6.25, $p = 0.031$), and 2 years (49.54 ± 4.99 vs. 46.12 ± 7.84, $p = 0.045$) after IMRT.

Figure 5B shows longitudinal and cross-sectional changes in MCS by age in patient with IMRT alone. Levels of MCS increased over time in young patients, reaching a significant peak 6 months after IMRT (47.95 ± 6.78 vs. 51.69 ± 4.47, $p = 0.050$). The MCS for older patients was highest 3 months after IMRT. However, no significant longitudinal changes were observed over the 3-years follow-up period.

Up to 3 years after IMRT, there were no cross-sectional differences in MCS between younger and older patients.

Patients Treated with IMRT Combined with ADT

No significant change was observed in the PCS, which decreased up to 6 weeks after IMRT and then increased in younger patients (Figure 6A). By contrast, older patients had the highest baseline PCS score of 50.64 ± 5.90. Although no significant difference was observed up to 3 years, PCS continued to decline. A comparison of PCS between younger and older patients revealed that PCS was significantly higher in younger patients at both 2 (50.03 ± 5.11 vs. 46.92 ± 6.99, $p = 0.0022$) and 3 years (50.04 ± 5.94 vs. 46.45 ± 8.23, $p = 0.033$) following IMRT.



6A: Average Summary Scores for Physical Health (PCS)

6B: Average Summary Scores for Mental Health (MCS)

Figure 6: Longitudinal and Cross-Sectional Evaluations of Average Summary Score for Health according to Age in Patients treated with Intensity Modulated Radiotherapy (IMRT) combined with Androgen Deprivation Therapy (ADT)
N.S: No statistically significant changes longitudinally compared with baseline

Regarding MCS, it was significantly higher in younger patients than in older patients 6 months after IMRT (52.63 ± 4.37 vs. 51.08 ± 5.67, p = 0.050). However, no longitudinal changes were observed regardless of age (Figure 6B).

Discussion

This study is characterized by its analysis of changes in PCS and MCS in a relatively large cohort of 267 patients with localized prostate cancer who received IMRT which is expected to reduce adverse events. The analysis uses longitudinal and cross-sectional methods and is based on data from a single institution. Notably, cross-sectional analyses reporting variations in PCS and MCS based on patient age, concomitant ADH use, and the duration of ADH administration are uncommon.

Many reports indicate that patients treated with external beam radiation therapy experience a significant decline in HRQOL, particularly PCS [14,18-21]. However, our analysis revealed no decline in PCS and MSC, with MSC showing a significant increase at 3 months after IMRT, which is thought to be due to the use of IMRT in radiation therapy. IMRT minimizes acute adverse events to the rectum, bladder, and urethra. The significant increase in MCS three months after IMRT may be considered to be due to the reduced influence of acute adverse events of radiation.

There are many reports indicating that PCS declines in patients undergoing external beam radiation therapy, and significantly inferior to the radical prostatectomy and brachytherapy, although no significant differences in MCS [22]. Yamamoto et al reported that PCS began to decrease at 3 months after IMRT and then returned to the baseline score at 24 months. They also reported, in contrast, the MCS score began to significantly increase after IMRT, and thereafter the score remained constant until 24 months [23]. On the other hand, Lane et al. reported physical and mental health were unaffected by IMRT or Brachytherapy [24].

The literatures which demonstrated that HRQOL of patients treated with EBRT deteriorated were contradict the results of our study. Since these reports lack details on the radiation therapy methods used, combination of ADT or the patients' ages, definitive conclusions are difficult to make. However, it is possible that the use of IMRT, the latest radiation therapy method, reduced the frequency and severity of adverse events in our study patients, thereby preventing a deterioration in HRQOL. In the prospective, longitudinal, observational study which published by Maggio et al., high radiation IMRT doses delivered for prostate cancer led to a temporary worsening of HRQOL was mostly associated with acute gastrointestinal and/or genitourinary toxicities, prophylactic lymph-nodal irradiation, and higher prescription doses [25]. Namiki and Arai reviewed that HRQOL of Japanese men treated with IMRT was better than that of men treated with conventional or conformal radiotherapy for 2 years after the therapy in their review article [6]. Progress in radiation treatment modalities is progressively and Intensity modulated proton therapy (IMPT) and C-ion radiotherapy is employed in clinical use of localized prostate cancer especially in Japan. Proton beam therapy had less acute decrement in bowel function domain than IMRT following radiotherapy. There was no difference between the two modalities in urinary domains [26]. Ishikawa et al. reported PCS slightly decreased with the passage of time, and the score at 12 months after initiation of C-ion RT was significantly worse than that at baseline. In contrast, MCS scores at all three points after C-ion RT were maintained in comparison to the corresponding baseline scores [27].

Some researchers demonstrated that the deterioration of MCS was marked in the early period after ADT, but there was a definite recovery trend over time [22,28]. On the other hand, Joly et al. also reported that patients treated with ADT who complain more decline of physical quality of life [14]. No remarkable declines in PCS or MCS were observed in patients treated with ADT compared with baseline levels in Japanese men [29]. The association of ADT and external beam radiation therapy decreases HRQOL of the patients, with a negative impact on vitality, sexuality and increase urinary disorder 14). Heer and O'Sullivan compared patients receiving ADT and those with asymptomatic advanced cancer [30]. They documented better HRQOL among patients who opted to defer treatment as compared with those who opted for early interventions. Potosky et al. studied HRQOL in patients with localized prostate cancer who were treated initially with ADT or not treated reported that protracted ADT was associated with worse physical function and more fatigue as compared with patients receiving no therapy [31]. Ishikawa et al. concludes that a probable reason for the tendency of PCS scores to be lower 12 months after C-ion RT compared to baseline in their study is that their study included 70 (92%) out of 76 patients who received ADT combined with C-ion RT [27]. On the other hand, Lubeck et al. stated that patients on ADT did not exhibit any noticeable decrements in the scores of the general HRQOL at one year after therapy [32]. With regard to Japanese subjects,

almost all HRQOL measures except for sexual function were mostly unaffected by ADT [33]. In the present study, although no significant differences were observed, patients receiving ADT had lower PCS. However, neither group showed any change in PCS over time, regardless of the administration of ADT. MCS was higher in patients treated with IMRT combined with ADT and showed a temporary significant decrease 4 weeks after the initiation of IMRT. However, it increased significantly 6 months after IMRT, regardless of ADT combination status.

Reports that compare HRQOL by treatment modalities among patients receiving different therapies often lack a detailed analysis of the selection criteria for each treatment, including patient age. This is also true for reports on radiotherapy patients.

The mean age for all of the 267 patients enrolled in this study was 71.5 years (range 53-82 years). Among the 165 older patients (61.8%), the mean age was 75.3 years, indicating an exceptionally advanced age compared to that of patients in previous studies who underwent localized prostate cancer treatment [24]. In current study, we divided the analysis into two groups to clarify how patient age affects changes in HRQOL among patients who underwent IMRT: younger patients (70 years or younger) and older patients (71 years or older). Among the older patients, PCS scores were lower than those of younger individuals across all evaluation points and a significant difference was observed at 5 out of 8 evaluation points, including the baseline score, with PCS being lower in older patients. A notable increase in MCS was observed among younger patients, with a delay of at least 3 months after the completion of IMRT. This may also be because the short-term ADT administered as adjuvant therapy prior to IMRT completion has ended, and the impact of ADT on mental health has diminished.

Previous studies have found that older age at the time of treatment is associated with lower HRQOL function scores after treatment [34,35]. However, Litwin et al. also reported that the mental health profiles of older men were better, even though the older men tended to be sicker. This may indicate that because older men start with lower baseline QOL scores, they have lower recovery expectations than younger patients, or that older patients have developed greater resilience to QOL fluctuations over time [21]. Age and comorbidities were found to be relevant for baseline scores, but not for score changes [20].

The mental health profiles differ for patients undergoing surgery, radiation, or watchful waiting for early stage prostate cancer. Patients with more serious disease, as evidenced by higher PSA levels or more aggressive histology, tended to worry more about it. Older men performed better, while sicker men performed worse, even though the older men tended to be sicker [21].

Hampson et al. also reported age is associated with all quality of life (QOL) scores, except for mental health scores, which decline in older adults. Their data confirm that older men had lower unadjusted QOL scores both before and after treatment for all domains except mental health [36]. However, in the current study, we were unable to confirm that MCS decreases in older patients, despite the fact that it increased in younger patients.

Conclusion

The deterioration of HRQOL in patients with localized prostate cancer was minimized by reducing of adverse events with IMRT. However, age and ADT influenced changes in PCS and MCS. Therefore, when evaluating changes in HRQOL associated with external beam radiation therapy for patients with localized prostate cancer, it is important to consider the type of radiation therapy, the patient's age, and whether they are receiving concomitant ADT, as well as how long they have been receiving it.

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